

Please type a plus sign (+) inside this box →

PTO/SB/01 (12-97)

Approved for use through 9/30/00. OMB 0651-0032

Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

**DECLARATION FOR UTILITY OR
DESIGN
PATENT APPLICATION
(37 CFR 1.63)**

Declaration Submitted with Initial Filing Declaration Submitted after Initial Filing (surcharge (37 CFR 1.16 (e)) required)

Attorney Docket Number	426.97.265
First Named Inventor	DeWitte
COMPLETE IF KNOWN	
Application Number	09 / 220,363
Filing Date	December 24, 1998
Group Art Unit	Not Assigned
Examiner Name	Not Assigned

As a below named Inventor, I hereby declare that:

My residence, post office address, and citizenship are as stated below next to my name.

I believe I am the original, first and sole Inventor (if only one name is listed below) or an original, first and joint Inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

**System and Method for Structure-Based Drug Design That
Includes Accurate Prediction of Binding Free Energy**

the specification of which

(Title of the Invention)

is attached hereto

OR

was filed on (MM/DD/YYYY) as United States Application Number or PCT International

Application Number and was amended on (MM/DD/YYYY) (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment specifically referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR 1.56.

I hereby claim foreign priority benefits under 35 U.S.C. 119(a)-(d) or 365(b) of any foreign application(s) for patent or Inventor's certificate, or 365(a) of any PCT International application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent or Inventor's certificate, or of any PCT International application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application Number(s)	Country	Foreign Filing Date (MM/DD/YYYY)	Priority Not Claimed	Certified Copy Attached?
			<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/>
			<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/>
			<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/>
			<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/>

Additional foreign application numbers are listed on a supplemental priority data sheet PTO/SB/02B attached hereto:

I hereby claim the benefit under 35 U.S.C. 119(e) of any United States provisional application(s) listed below.

Application Number(s)	Filing Date (MM/DD/YYYY)	
		<input type="checkbox"/> Additional provisional application numbers are listed on a supplemental priority data sheet PTO/SB/02B attached hereto.

[Page 1 of 4]

Burden Hour Statement: This form is estimated to take 0.4 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

Please type a plus sign (+) inside this box →

PTO/SB/01 (12-97)

Approved for use through 9/30/00. OMB 0651-0032

Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

DECLARATION — Utility or Design Patent Application

I hereby claim the benefit under 35 U.S.C. 120 of any United States application(s), or 365(c) of any PCT international application designating the United States of America, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT international application in the manner provided by the first paragraph of 35 U.S.C. 112, I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application.

U.S. Parent Application or PCT Parent Number	Parent Filing Date (MM/DD/YYYY)	Parent Patent Number (if applicable)
08/741,866	09/26/96	

Additional U.S. or PCT International application numbers are listed on a supplemental priority data sheet PTO/SB/02B attached hereto.

As a named Inventor, I hereby appoint the following registered practitioner(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith: Customer Number → Place Customer Number Bar Code Label here
 OR
 Registered practitioner(s) name/registration number listed below

Name	Registration Number	Name	Registration Number
Keum J. Park	42,059		

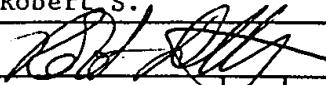
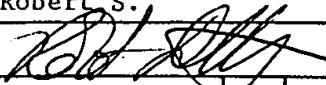
Additional registered practitioner(s) named on supplemental Registered Practitioner Information sheet PTO/SB/02C attached hereto.

Direct all correspondence to: Customer Number OR Correspondence address below

Name	Keum J. Park					
Address	Hale and Dorr LLP					
Address	60 State Street					
City	Boston	State	MA	ZIP	02109	
Country	USA	Telephone	617-526-6110	Fax	617-526-5000	

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Name of Sole or First Inventor: A petition has been filed for this unsigned inventor

Given Name (first and middle if any)			Family Name or Surname				
Robert S. 			DeWitte				
Inventor's Signature						Date	3-9-99
Residence: City	Gurnee	State	IL	Country	USA	Citizenship	Canada
Post Office Address	1518 Almaden Lane						
Post Office Address							
City	Gurnee	State	IL	ZIP	60031	Country	USA

Additional inventors are being named on the 1 supplemental Additional Inventor(s) sheet(s) PTO/SB/02A attached hereto

Please type a plus sign (+) inside this box → Approved for use through 9/30/98. OMB 0651-0032
Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

DECLARATION

ADDITIONAL INVENTOR(S)
Supplemental Sheet
Page 1 of 1

Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this unsigned inventor					
Given Name (first and middle [if any])				Family Name or Surname			
Eugene I.				Shakhnovich			
Inventor's Signature							Date
Residence: City	Lexington	State	MA	Country	USA	Citizenship	USA
Post Office Address	16 Woodcliffe Road						
Post Office Address							
City	Lexington	State	MA	ZIP	02173	Country	USA
Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this unsigned inventor					
Given Name (first and middle [if any])				Family Name or Surname			
Inventor's Signature							Date
Residence: City		State		Country		Citizenship	
Post Office Address							
Post Office Address							
City		State		ZIP		Country	
Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this unsigned inventor					
Given Name (first and middle [if any])				Family Name or Surname			
Inventor's Signature							Date
Residence: City		State		Country		Citizenship	
Post Office Address							
Post Office Address							
City		State		ZIP		Country	

Burden Hour Statement: This form is estimated to take 0.4 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

Please type a plus sign (+) inside this box →

PTO/SB/02C (3-97)

Approved for use through 9/30/98. OMB 0651-0032

Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

DECLARATION

REGISTERED PRACTITIONER INFORMATION (Supplemental Sheet)

Name	Registration Number	Name	Registration Number
James B. Lampert	24,564		
Wayne M. Kennard	30,271		
Michael J. Bevilacqua	31,091		
Hollie L. Baker	31,321		
Henry N. Wixon	32,073		
Anne-Louise Kerner	33,523		
Wayne A. Keown	33,923		
Michael A. Diener	37,122		
Donald R. Steinberg	37,241		
Gretchen A. Rice	37,429		
Peter M. Dichiara	38,005		
Richard A. Goldenberg	38,895		
Colleen Superko	39,850		
Scott M. Alter	32,879		
Barbara A. Barakat	32,190		
Edward D. Grieff	38,898		
Jason A. Reyes	41,513		
Rajesh Vallabh	35,761		

Burden Hour Statement: This form is estimated to take 0.4 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

[Page 4 of 4]

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

**DECLARATION FOR UTILITY OR
DESIGN
PATENT APPLICATION
(37 CFR 1.63)**

Declaration Submitted with Initial Filing Declaration Submitted after Initial Filing (surcharge (37 CFR 1.16 (e)) required)

Attorney Docket Number	426.97.265
First Named Inventor	DeWitte
COMPLETE IF KNOWN	
Application Number	09 / 220,363
Filing Date	December 24, 1998
Group Art Unit	Not Assigned
Examiner Name	Not Assigned

As a below named Inventor, I hereby declare that:

My residence, post office address, and citizenship are as stated below next to my name.

I believe I am the original, first and sole Inventor (if only one name is listed below) or an original, first and joint Inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

**System and Method for Structure-Based Drug Design That
Includes Accurate Prediction of Binding Free Energy**

the specification of which

(Title of the Invention)

is attached hereto

OR

was filed on (MM/DD/YYYY) as United States Application Number or PCT International

Application Number and was amended on (MM/DD/YYYY) (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment specifically referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR 1.56.

I hereby claim foreign priority benefits under 35 U.S.C. 119(a)-(d) or 365(b) of any foreign application(s) for patent or Inventor's certificate, or 365(a) of any PCT International application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent or Inventor's certificate, or of any PCT International application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application Number(s)	Country	Foreign Filing Date (MM/DD/YYYY)	Priority Not Claimed	Certified Copy Attached?
			<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>

Additional foreign application numbers are listed on a supplemental priority data sheet PTO/SB/02B attached hereto:

I hereby claim the benefit under 35 U.S.C. 119(e) of any United States provisional application(s) listed below.

Application Number(s)	Filing Date (MM/DD/YYYY)	Additional provisional application numbers are listed on a supplemental priority data sheet PTO/SB/02B attached hereto.

[Page 1 of 4]

Burden Hour Statement: This form is estimated to take 0.4 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

Please type a plus sign (+) inside this box →

PTO/SB/01 (12-97)

Approved for use through 9/30/00. OMB 0651-0032

Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

DECLARATION — Utility or Design Patent Application

I hereby claim the benefit under 35 U.S.C. 120 of any United States application(s), or 365(c) of any PCT International application designating the United States of America, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of 35 U.S.C. 112, I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR 1.56 which became available between the filing date of the prior application and the national or PCT International filing date of this application.

U.S. Parent Application or PCT Parent Number	Parent Filing Date (MM/DD/YYYY)	Parent Patent Number (if applicable)
--	---------------------------------	--------------------------------------

08/741,866	09/26/96	
------------	----------	--

Additional U.S. or PCT International application numbers are listed on a supplemental priority data sheet PTO/SB/02B attached hereto.

As a named Inventor, I hereby appoint the following registered practitioner(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith: Customer Number → Place Customer Number Bar Code Label here
OR
 Registered practitioner(s) name/registration number listed below

Name	Registration Number	Name	Registration Number
Keum J. Park	42,059		

Additional registered practitioner(s) named on supplemental Registered Practitioner Information sheet PTO/SB/02C attached hereto.

Direct all correspondence to: Customer Number or Bar Code Label OR Correspondence address below

Name	Keum J. Park				
Address	Hale and Dorr LLP				
Address	60 State Street				
City	Boston	State	MA	ZIP	02109
Country	USA	Telephone	617-526-6110		Fax 617-526-5000

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Name of Sole or First Inventor:	<input type="checkbox"/> A petition has been filed for this unsigned inventor						
Given Name (first and middle if any)			Family Name or Surname				
Robert S.			DeWitte				
Inventor's Signature						Date	
Residence: City	Gurnee	State	IL	Country	USA	Citizenship	Canada
Post Office Address	1518 Almaden Lane						
Post Office Address							
City	Gurnee	State	IL	ZIP	60031	Country	USA

Additional inventors are being named on the 1 supplemental Additional Inventor(s) sheet(s) PTO/SB/02A attached hereto

Please type a plus sign (+) inside this box →

Approved for use through 9/30/98. OMB 0651-0032

Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

DECLARATION

ADDITIONAL INVENTOR(S)
Supplemental Sheet
Page 1 of 1

Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this unsigned inventor					
Given Name (first and middle [if any])			Family Name or Surname				
Eugene I.			Shakhnovich				
Inventor's Signature						3-23-99 Date	
Residence: City	Lexington	State	MA	Country	USA	Citizenship	USA
Post Office Address	16 Woodcliffe Road						
Post Office Address							
City	Lexington	State	MA	ZIP	02173	Country	USA
Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this unsigned inventor					
Given Name (first and middle [if any])			Family Name or Surname				
Inventor's Signature						Date	
Residence: City		State		Country		Citizenship	
Post Office Address							
Post Office Address							
City		State		ZIP		Country	
Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this unsigned inventor					
Given Name (first and middle [if any])			Family Name or Surname				
Inventor's Signature						Date	
Residence: City		State		Country		Citizenship	
Post Office Address							
Post Office Address							
City		State		ZIP		Country	

Burden Hour Statement: This form is estimated to take 0.4 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

[Page 3 of 4]

Please type a plus sign (+) inside this box →

PTO/SB/02C (3-97)

Approved for use through 9/30/98. OMB 0651-0032

Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a
valid OMB control number.

DECLARATION

REGISTERED PRACTITIONER INFORMATION (Supplemental Sheet)

Name	Registration Number	Name	Registration Number
James B. Lampert	24,564		
Wayne M. Kennard	30,271		
Michael J. Bevilacqua	31,091		
Hollie L. Baker	31,321		
Henry N. Wixon	32,073		
Anne-Louise Kerner	33,523		
Wayne A. Keown	33,923		
Michael A. Diener	37,122		
Donald R. Steinberg	37,241		
Gretchen A. Rice	37,429		
Peter M. Dichiara	38,005		
Richard A. Goldenberg	38,895		
Colleen Superko	39,850		
Scott M. Alter	32,879		
Barbara A. Barakat	32,190		
Edward D. Grief	38,898		
Jason A. Reyes	41,513		
Rajesh Vallabh	35,761		

Burden Hour Statement: This form is estimated to take 0.4 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

[Page 4 of 4]

ASSIGNMENT

COPY

WHEREAS, I, Robert S. DeWitte, being a citizen of Canada, residing at 1518 Almaden Lane, Gurnee, IL 60031, and Eugene I. Shakhnovich, residing at 16 Woodcliffe Road, Lexington, MA 02173, am an inventor of certain new and useful inventions and discoveries, for which I have made an application for Letters Patent entitled System and Method for Structure-Based Drug Design That Includes Accurate Prediction of Binding Free Energy, U.S. Serial No. 09/220,363, a declaration for which I have executed on an even day; and

WHEREAS, Harvard University, a University whose address is University Place, 124 Mt. Auburn Street, Cambridge, MA 02138, and which, together with its successors and assigns is hereinafter called "ASSIGNEE," is desirous of acquiring the title, rights, benefits, and privileges hereinafter recited;

NOW, THEREFORE, for and in consideration of good and valuable consideration furnished by ASSIGNEE to me, receipt and sufficiency of which I hereby acknowledge, I hereby, without reservations:

1. Assign, transfer, and convey to ASSIGNEE the entire right, title, and interest in and to said inventions and discoveries, said application for Letters Patent, any and all other applications for Letters Patent on said inventions and discoveries in whatsoever countries, including all divisional, renewal, substitute, continuation, continuation-in-part, and convention applications based in whole, or in part, upon said inventions or discoveries, or upon said applications, and any and all Letters Patents, reissues, and extensions of Letters Patent granted for said inventions and discoveries or upon said applications, and every priority right that is or may be predicated upon, or arise from, said inventions, said discoveries, said applications, and said Letters Patent;

2. Authorize ASSIGNEE to file patent applications in any or all countries on any or all of said inventions and discoveries in my name or in the name of

ASSIGNEE or otherwise as ASSIGNEE may deem advisable, under International Conventions or otherwise;

3. Authorize and request the Commissioner of Patents and Trademarks of the United States of America and the empowered officials of all other governments throughout the world to issue or transfer all said Letters Patents to ASSIGNEE, as assignee of the entire right, title, and interest therein or otherwise as ASSIGNEE may direct;

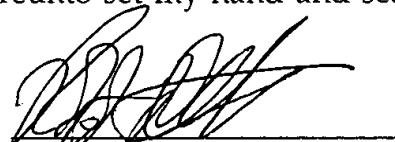
4. Warrant that I have not knowingly conveyed to others any right in said inventions, discoveries, applications, or patents, or any license to use the same, or to make, use, or sell anything embodying or utilizing any of said inventions or discoveries; and that I have good right to assign the same to ASSIGNEE without encumbrance;

5. Bind my heirs, legal representatives, and assigns, as well as myself, to do, upon ASSIGNEE's request and at ASSIGNEE's expense, but without additional consideration to me or them, all acts reasonably serving to assure that said inventions and discoveries, said patent applications, and said Letters Patents shall be held and enjoyed by ASSIGNEE as fully and entirely as the same could have been held and enjoyed by me, our heirs, legal representatives, and assigns if this Assignment had not been made; and particularly to execute and deliver to ASSIGNEE all lawful application documents including petitions, specifications, and oaths, and all assignments, disclaimers, and lawful affidavits in form and substance as may be requested by ASSIGNEE; and to communicate to ASSIGNEE all facts known to me relating to said inventions and discoveries or the history thereof, and to testify as to the same in any court or proceeding; and to furnish ASSIGNEE any and all documents, photographs, models, samples, and other physical exhibits in my control or in the control of my heirs, legal representatives, or assigns which may be useful

for establishing the facts of my conceptions, disclosures, and reduction to practice of
said inventions and discoveries.

IN TESTIMONY WHEREOF, I have hereunto set my hand and seal.

DATE: Mar 9/99



Robert S. DeWitte

WITNESSED BY:

Michelle K. DeWitte
Name

Michelle K. DeWitte

1518 Almada Ln
Gurnee IL 60031
Address

DATE: Mar 9/99

DATE: _____

Eugene I. Shakhnovich

WITNESSED BY:

Name

Address

DATE: _____

for establishing the facts of my conceptions, disclosures, and reduction to practice of said inventions and discoveries.

IN TESTIMONY WHEREOF, I have hereunto set my hand and seal.

DATE: _____

Robert S. DeWitte

WITNESSED BY:

Name

Address

DATE: _____

DATE: 3-23-99



Eugene I. Shakhnovich

WITNESSED BY:

Patricia Gall

Name

Harvard University
Mallinckrodt B9-33
12 Oxford Street
Cambridge, MA 02138

Address

DATE: 3-23-99